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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,343	07/23/2007	Holger Zimmermann	BHC 03 1095	4690

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EXAMINER	
SHTERENGARTS, SAMANTHA L	
ART UNIT	**PAPER NUMBER**
1626	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,343	ZIMMERMANN ET AL.	
	Examiner	Art Unit	
	SAMANTHA SHTERENGARTS	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *26 Sept 06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-10 are currently pending in the instant application.

Priority

2. The instant application is a national stage entry of PCT/EP2005/002571, filed on March 11, 2005, which claims priority to German Patent No. 10 2004 015 007.9, filed March 26, 2004.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on September 26, 2006 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS document was considered. A signed copy of form 1449 is enclosed herewith.

Claim Objections

4. Claim 10 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on 5 claims in the alternative. See MPEP § 608.01(n). Accordingly, the claim not been further treated on the merits.

Claim Rejections - 35 USC § 112

(First Paragraph)

5. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutically acceptable salts, does not reasonably provide enablement for pharmaceutically acceptable solvates and for solvates of the salts thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The Nature of the Invention

The nature of the invention is the compounds of Formula (I) and their pharmaceutically acceptable salts, solvates, and solvates of their pharmaceutically acceptable salts.

The State of the Prior Art and the Predictability or lack thereof in the art

Active pharmaceutical ingredients are frequently delivered to the patient in the solid-state as part of an approved dosage form (e.g., tablets, capsules, etc.). Solids provide a convenient, compact, and generally stable format to store an active pharmaceutical ingredient or a drug product. Understanding and controlling the solid-state chemistry of active pharmaceutical ingredients, both as pure drug substances and in formulated products, is therefore an important aspect of the drug development process. Active pharmaceutical ingredients can exist in a variety of distinct solid forms, including polymorphs, solvates, hydrates, salts, co-crystals, and amorphous solids. Each form displays unique physicochemical properties that can profoundly influence the bioavailability, manufacturability purification, stability, and other performance characteristics of the drug. Hence, it is critical to understand the relationship between the particular solid form of a compound and its functional properties.

For ionizable compounds, preparation of salt forms using pharmaceutically acceptable acids and bases is a common strategy to improve bioavailability. However, the preparation of other solid forms such as polymorphs, solvates, and hydrates, are not so common to be predictable. In order to obtain patent protection on these forms, some of which may have significantly different properties and relevance as development candidates, it is essential to prepare them, identify conditions for making them, and evaluate their properties as valuable new pharmaceutical materials. A large number of factors can influence crystal nucleation and growth during this process, including the composition of the crystallization medium and the processes

used to generate super-saturation and promote crystallization (Morissette et al. Advanced Drug Delivery Reviews 2004, 56, 275-300). Therefore, for these reasons, the state of the prior art is one of unpredictability.

As stated above, crystalline solids can exist in the form of polymorph, solvates or hydrates. "Phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate, and conversion of crystalline to amorphous form may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug. Hence, it is desirable to choose the most suitable and stable form of the drug in the initial stages of drug development" (Vippagunta et al., abstract, Vippagunta, Sudha R. "Crystalline Solids." Advanced Drug Delivery Reviews 48(2001): 3-26.) In further discussing the predictability of the formation of solvates, Vippagunta et al. discloses that "predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds" (page 18, section 3.4).

The Amount of Direction or Guidance Present and Presence or Absence of Working Examples

The only direction or guidance present in the instant specification is in ¶[0035], where it is discloses that, "Solvates refer for the purposes of the invention to those forms of the compounds of the invention which form a complex in the solid or liquid state by coordination with solvent molecules. Hydrates are a special form of solvates in which the coordination takes place with water." This definition does not enable one to make and use solvates of each embodiment of the instantly claimed compound. There is no data present in the specification for

the preparation of solvates of compounds of the Formula (I). It is not discussed which specific compounds can exist in these forms. Finally, there are no working examples present in the disclosure for the preparation of solvates.

The Breadth of the Claims

The instant breadth of the rejected claims is broader than the disclosure, specifically; the instant claims include any solvates of the claimed compounds.

The Quantity of Experimentation Needed and the Level of Skill in the Art

While the level of skill in the pharmaceutical arts is high, it would require undue experimentation for one of ordinary skill in the pertinent art to prepare *any* solvate of the compounds of Formula (I). The science of crystallization has evolved such that, without guidance or working examples in the specification, the claims lack enablement.

6. Claims 5 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Nature of the Invention

Claim 5 is drawn to a compound for the treatment and/or prophylaxis of diseases and claim 9 is drawn to a medicament according to claim 6 for the treatment and/or prophylaxis of viral infections.

The prophylactic treatment or "prevention" actually means to anticipate or counter in advanced, to keep from happening, etc. and there is no disclosure as to how one skilled in the art

can reasonably establish the basis and the type of subject to which the instant compounds, compositions, and medicaments can be administered in order to have the "preventative" effect.

The State of the Prior Art and the Predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic preventative regimen on its face.

The instantly claimed invention is highly unpredictable as discussed below: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that the instantly claimed compounds are not enabled for treating and preventing all diseases, or even all viral infections.

Applicant's claims are drawn to the treatment and prevention of all diseases, as well as the treatment and prevention of viral infections. Viral infections include, but are not limited to: AIDS, AIDS Related Complex, HIV, Chickenpox (Varicella), Common cold, Cytomegalovirus Infection, Colorado tick fever, Dengue fever, Ebola hemorrhagic fever, Hand, foot and mouth disease, Hepatitis, Herpes simplex, Herpes zoster, HPV, Influenza (Flu), Lassa fever, Measles, Marburg hemorrhagic fever, Infectious mononucleosis, Mumps, Norovirus, Poliomyelitis,

Progressive multifocal leukencephalopathy, Rabies, Rubella, SARS, Smallpox (Variola), Viral encephalitis, Viral gastroenteritis, Viral meningitis, Viral pneumonia, West Nile disease, and Yellow fever.

With regards to HIV, for example, HIV (human immunodeficiency virus) damages and destroys the cells of your immune system, interfering with your body's ability to effectively fight off viruses, bacteria, and fungi. In terms of prevention, there is no vaccine to prevent HIV infection and no cure for AIDS (caused by HIV). Prevention of HIV includes education, protection, caution, and testing.

http://www.mayoclinic.com/health/hiv-aids/DS00005

The challenge of preventing HIV has been determining target specific therapies. The symptoms and causes are too divergent and some are still unknown, and therefore require education as a preventative measure. There is no common mechanism by which all persons infected with HIV can rely on. Likewise, for HIV-negative persons, there is no preventative medicament available. Applicant's disclosure does not enable one of ordinary skill in the art to make or use the claimed invention within the entire scope of the diseases listed above.

The amount of direction or guidance present and the presence or absence of working examples

The specification does not contain any evidentiary support or working examples to support the treatment and prevention of all diseases, or the entire class of viral infections.

The breadth of the claims

The claims are broader than what is supported by the disclosure, as they are drawn to a method of treating and preventing all diseases, and all disease encompassed by the class of viral infections.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the inventions is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compound exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the treatment and prevention of all diseases (as in instant claim 5), or all viral infections (as in instant claim 9), as a result necessitating one of skill to perform an exhaustive search for which compounds of the instant claims will be useful in order to practice the claimed invention.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what compounds, out of all compounds, would be effective in treating and preventing diseases and viral infections.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. nave been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which compositions would treat and prevent diseases, which diseases they are, and viral infections, and which viral infections they are, with no assurance of success.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 7-8 are rejected because the claimed invention is directed to non-statutory subject matter and because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 7-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established

utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samantha Shterengarts whose telephone number is (571)270-5316. The examiner can normally be reached on Monday thru Thursday, 9AM – 6PM Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Cecilia Tsang and Janet Andres can be reached on 571-272-0562 and 571-272-0867, respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAMANTHA SHTERENGARTS/
Examiner, Art Unit 4131

/Kamal A Saeed/
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